Draft 2-15-2007 Action Plan
To Develop the Toxicity Assessment
for Libby Amphibole

Objectives

The primary objective of this Action Plan is to provide a list of studies that will support the development of a toxicity assessment for the mixture of fibrous amphibole minerals found in Libby, Montana ("Libby Amphibole"). This toxicity assessment coupled with an exposure assessment will comprise the baseline risk assessment that is needed to support a Record of Decision (ROD) for the Libby site. This Action Plans provides a recommended list of studies, the organization that would perform each of them, and cost estimates. This Action Plan also recommends studies of analytical methods, which are critical to the exposure assessment. A longer-term research program is also recommended to further improve understanding of the human effects from low-level exposure to Libby Amphibole and other asbestos-like mineral fibers. Finally, Region 8 has requested establishment of a human tissue repository and expansion of the Libby medical monitoring program. These latter requests are beyond the scope of this action plan which is focused on the critical studies needed to support a ROD for the Libby site. OSWER will request further consultation with ATSDR and Region 8 on these additional requests.

Background

In order to determine a comprehensive and protective Libby site remedy, EPA must complete a baseline risk assessment. The studies included in this Action Plan are designed to address some of the areas of scientific uncertainty that are associated with the toxicity and health risks of the Libby Amphibole. On January 17 and 18, 2007, a meeting was held with EPA and other federal scientists to identify data gaps that need to be addressed to support an assessment of human health risk stemming from exposure to Libby Amphibole. The group developed a list of studies that are needed and their relative priorities in terms of completing the Libby toxicity assessment. At this meeting, a Steering Committee was established to develop this draft action plan. Members of this Steering Committee included representatives from ORD/NHEERL, ORD/NCEA, OSWER, and Region 8. The Steering Committee developed more detailed descriptions of each study, which are summarized below.

Toxicity Assessment Support Studies

a) ***Libby Amphibole RfC Development***. Dr. Robert Benson with Region 8 is developing a site-specific RfC (the non-cancer toxicity value) for Libby Amphibole based primarily on epidemiological information from the Marysville, Ohio cohort who were exposed to Libby Amphibole. NCEA will assist by evaluate options for quantitative analysis of the Marysville, Ohio

cohort including additional statistical support. Additionally, a human dosimetry model, constructed by ORD/NHEERL, will be used to predict internal dose and will be integrated into the site-specific RfC. This site-specific product will be subject to external peer review. NCEA will provide assistance with the peer review process

b) ***Libby Amphibole Cancer Assessment.*** ORD/NCEA will conduct a cancer assessment specifically for Libby Amphibole for the Integrated Risk Information System (IRIS). As with all IRIS assessments, available studies (epidemiologic and animal toxicity) will be considered, as well as models both for dosimetry and risk assessment. This effort will go through Agency and Interagency review as a standard assessment for the EPA's Integrated Risk Information System (IRIS).

c) ***USGS Preparation of Libby Testing Material.*** USGS will collect, prepare, and thoroughly characterize material from the Libby mine (under an Interagency Agreement with Region 8). This material will be used in the ORD/NHEERL laboratory animal toxicity studies and the analytical method studies.

d) ***Fiber Size Distribution in Libby Vermiculite.*** Region 8 will verify the fiber size distribution of Libby Amphibole fibers entrained from Libby vermiculite. This work is necessary to support the site-specific Reference Concentration (RfC) in development.

e) ***NHEERL Dosimetry Model Development and Simulation Studies.*** ORD/NHEERL will develop a dosimetry model using existing data and available equations for deposition and clearance based on general fiber dimensions. This model will allow for estimation of internal tissue dose (lung burden) in a generic sense but will need to be updated with Libby Amphibole-specific data. A dosimetry model will allow quantitative prediction of internal dose across species to facilitate improved understanding of the exposure-response in humans.

f) ***NHEERL In Vitro Dissolution Assays.*** ORD/NHEERL will evaluate key physicochemical parameters of clearance mechanisms to refine the dosimetry model predictions of retained dose. The study is designed to make use of a vast existing NHEERL database on the dissolution and potency of asbestos and other similar fibers.

g) ***NHEERL In Vitro Toxicity Endpoints.*** ORD/NHEERL will evaluate potential key events and endpoints (e.g., cytotoxicity, oxidative burden, genotoxicity) for known asbestos samples of Libby Amphibole and other better studied fibers.

h) ***NHEERL Comparative Toxicology in Mice and Rats.*** ORD/NHEERL will conduct animal studies to determine the relative potency of Libby Amphibole compared to other types of asbestos; evaluate non-respiratory endpoints; and evaluate the potential for an increased susceptibility for children by examining, in utero (infantile) and early lifetime dosing vs. adult animal treatment. These studies will be applied to the dosimetry model.

i) ***NHEERL Inhalation Toxicology in Rats.*** ORD/NHEERL, through a contract with the Hamner Institutes for Health Science (formerly CIIT), will conduct a 90-day inhalation study (followed by various holding times) in the rat to examine a variety of toxicological endpoints. This study will also examine the relationship between duration of exposure and the nature and persistence of effects. The study will provide key data for the dosimetry model as well as long-term effects.

j) ***New Epidemiologic Information from Libby Montana Cohort.*** The Region 8 Technical Team and NCEA will review recently available WR Grace information concerning historical worker asbestos exposures and associated asbestos-related abnormalities (pleural plaques, diffuse pleural thickening, asbestosis). This information will be included in the ongoing and future NIOSH cohort updates and may include extended morbidity investigation of former WR Grace workers to evaluate the exposure-response relationship; review and incorporate NIOSH mortality information; and evaluate biomarker data. Additionally, lung tissue collection will be pursued to improve the understanding of Libby Amphibole exposure and lung fiber deposition dosimetry and to support exposure-response modeling.

k) ***New Epidemiologic Information from Other Cohorts.*** NCEA and Region 8 will work with NIOSH and ATSDR to develop epidemiologic information from other cohorts exposed to Libby Amphibole.

l) ***OSWER Interim Risk Methodology for Quantification of Cancer Risk from Inhalation Exposure to Asbestos***. OSWER is developing a methodology for estimating the risk of lung cancer and mesothelioma from inhalation exposure to different forms of asbestos. This methodology combines data from epidemiological exposure response studies with surrogate estimates of exposure (based on Transmission Electron Microscopy, TEM) that characterizes both the fiber type and dimensions. Use of this draft interim risk assessment methodology will allow for estimates of risks of these effects for a variety of complex mixtures of asbestos materials. A consultation with the EPA Science Advisory Board on the models is planned for FY07.

Analytical Methods Studies

The following analytical methods studies have been identified by Region 8 as essential to supporting the exposure assessment for Libby. Region 8 will have the lead for the

verification studies. OSRTI will provide the assistance of the Environmental Response Team to help expedite this work. Additional support may also be helpful from ORD and the Technical Review Work Group-Asbestos Committee.

m) ***Filter Verification.*** This study will evaluate air sampling methods including filter pore size (0.45 μm and 0.8 μm) and filter composition comparisons. Nearly all air samples collected in Libby have been collected on a 0.8 μm pore size filter but there is a concern that there may be a lower collection efficiency for the small potentially more toxic fibers. The study will also evaluate differences, if any, in data collected from the different filter types.

n) ***Low-Level Soil Method Development.*** This study will develop an analytical method to assess the presence or absence of Libby Amphibole in soil at levels less than ~0.05% (by weight). The study will attempt to validate Region 10's Glove Box method as applied to reference materials of Libby soil containing known amounts of Libby Amphibole. A validated method will provide a rapid and inexpensive screening tool to determine where more expensive alternatives such as activity-based sampling should be used at properties. Following validation of the Glove Box method, further development of a direct method for qualitative (presence/absence) identification of Libby Amphibole in soil will be performed.

o) ***Comparison of Direct & Indirect Preparations.*** This study will evaluate whether differences exist in fiber size distribution and/or total Libby Amphibole concentrations resulting from direct and indirect sample preparations. The study will address concerns about whether data from air samples prepared differently are comparable.

p) ***Ambient Air Collection Method Verification.*** This study will validate air sample collection techniques currently being used for the outdoor ambient air monitoring program.

Additional Project Planning, Agency Review, Interagency Consultation, and Peer Review

After the action plan has been tentatively approved based on initial funding estimates, additional project planning will be conducted by each lead organization. The project planning will include appropriate internal and external peer review and consultations with researchers in other federal agencies, especially ATSDR, NIOSH and NTP. Proposed projects will be expected to contain thorough literature reviews, supporting the technical approach. All draft work plans will be reviewed by the Technical Review Work Group-Asbestos Committee and will undergo external peer review. Final approval and funding may be modified based on these reviews and consultations.

A management committee with a representation for Region 8, OSWER, and ORD will be established to manage, track, and coordinate the overall effort. Because data from these studies must be useful for and applicable to the Libby Site, the Region 8 Team will be considered a crucial part of all efforts, including those studies for which they are not the designated lead.

Longer-Term Research Program

Several of the high priority data gaps (e.g., comprehensive PBPK model and intermittent exposure) identified at the January 17 and 18 meeting cannot be completely addressed within the timeframe identified for the toxicity assessment support studies. Given that response actions may not allow for unlimited use and unrestricted exposure at the Libby site and some scientific uncertainty will remain with the toxicity assessment, additional longer-term research will be critical to support five-year reviews at Libby and at other Libby Amphibole sites. A longer-term research program should also address toxicity issues associated with naturally occurring asbestos (NOA) fibers sites. We recommend that ORD establish a longer-term asbestos research program within its Superfund allocation of resources, to re-direct FTEs to this program. Given that the National Toxicology Program may be initiating an assessment of various NOAs, we believe ORD could benefit greatly from collaborating with NTP on asbestos research.

Funding/Resource Needs

The following table contains the funding needs for the toxicity assessment support studies and the analytical methods studies. FTE needs are not included; however, we anticipate that Region 8 and ORD will internally adjust their FTE to provide the necessary support.

FUNDING NEEDS	2007 $	2008 $	2009 $	Total $
TOXICITY ASSESSMENT SUPPORT STUDIES				
a. Region 8 Libby Amphibole RfC Development	25,000	-	75,000	100,000
b. NCEA Libby Amphibole Cancer Assessment	180,000	180,000	-	360,000
c. USGS Preparation of Libby Testing Material	150,000	150,000	-	300,000
d. Region 8 Fiber Size Distribution in Libby Vermiculite	-	90,000	-	90,000
e. NHEERL Dosimetry Model Development. Simulation Studies	135,000	75,000	-	210,000
f. NHEERL In Vitro Dissolution Assays	137,000	137,000	-	274,000
g. NHEERL In Vitro Toxicity Endpoints	247,500	247,500	-	495,000
h. NHEERL Comparative Toxicology in Mice and Rats	382,250	382,250	200,000	964,500
i. NHEERL Inhalation Toxicology in Rats	-	1,112,000	-	1,112,000
j. Region 8/NCEA New Epidemiologic Information from Libby Montana Cohort	335,000	180,000	180,000	695,000
k. NCEA New Epidemiologic Information from Other Cohorts	250,000	250,000	-	500,000
l. OSWER Interim Cancer Risk Methodology	-	-	-	-
TOTAL	1,841,750	2,803,750	455,000	5,100,500
ANALYTICAL METHODS STUDIES				
m. Region 8 Filter Verification Studies	650,000	-	-	650,000
n. Region 8 Low-Level Soil Method Development	-	230,000	-	230,000
o. Region 8 Comparison Direct & Indirect Preparations	-	350,000	-	350,000
p. Region 8 Ambient Air Collection Method Verification	450,000	-	-	450,000
TOTAL	1,100,000	580,000	-	1,680,000
GRAND TOTAL	2,941,750	3,383,750	455,000	6,780,500

Overall Schedule

The completion of the Libby risk assessment is expected in FY2010 based on initiation of these studies this fiscal year.

Milestones

- January 17 and 18, 2007 EPA and other federal scientists identify data gaps and studies to support the Libby Amphibole toxicity assessment
- February 12 -16, 2007 EPA managers review the proposed action plan
- February 12-16, 2007 Initiate funding levels approved
- February 19-23, 2007 Lead organizations develop study descriptions (based on funding)
- February 28, 2007 proposed study descriptions made available to the TAG expert
- March 6, 2007 meet with Libby Community Advisory Group/Technical Assistance Grant Group to present an overview of the toxicity assessment studies
- March 7, 2007 Town hall meeting in Libby, Montana
- April, 2007 finalize the detailed plans including a summary of existing literature and consultation with Technical Review Work Group-Asbestos Committee, other federal agencies, and external peer reviews
- May, 2007 initiate work
- May, 2007 (tentative) ORD scientists meet with Libby Community Advisory Group/Technical Assistance Grant Group to discuss details of studies
- Work products will be peer reviewed as they are completed.
- All data collection will be completed by Summer 2009